TRANSFUSION AND ARTERIAL ANASTOMOSIS.*

SOME EXPERIMENTS IN ARTERIAL ANASTOMOSIS AND A STUDY OF TRANSFUSION WITH PRESENTATION OF TWO CLINICAL CASES.

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THE brilliant experimental results of the past few years, in the anastomosis of blood vessels, are rapidly bringing this operation into the domain of practical surgery.

In September, 1906, it occurred to the author that it ought to be possible to unite blood vessels by means of a rigid ring, in such a way as to bring intima into direct contact with intima, and leave no foreign body in the lumen. With this idea in view, in the course of five trials on the cadaver and eight animal experiments, he developed a satisfactory technique.

Up to this time, he had been acquainted only with Carrel's articles on blood vessel suture. Now, a review of some experiments by Jaboulay,[1] led him to other references; and following up the literature of the subject, he found that the idea was not at all new, but had already been put in practice by a number of other experimenters.

Nevertheless, the author desires to present these experiments, not because they represent any new achievement, but because the lessons he learned might be of value to others who desire to enter this new field of surgery.

It was the experience thus gained, and an acquaintance with Crile's work on transfusion, that prompted the writer to perform direct transfusion when two desperate cases of anæmia presented themselves.

Of the author's eight animal experiments, the first four are disregarded, as the method was still in a developmental stage. Although of the last four experiments, only one was

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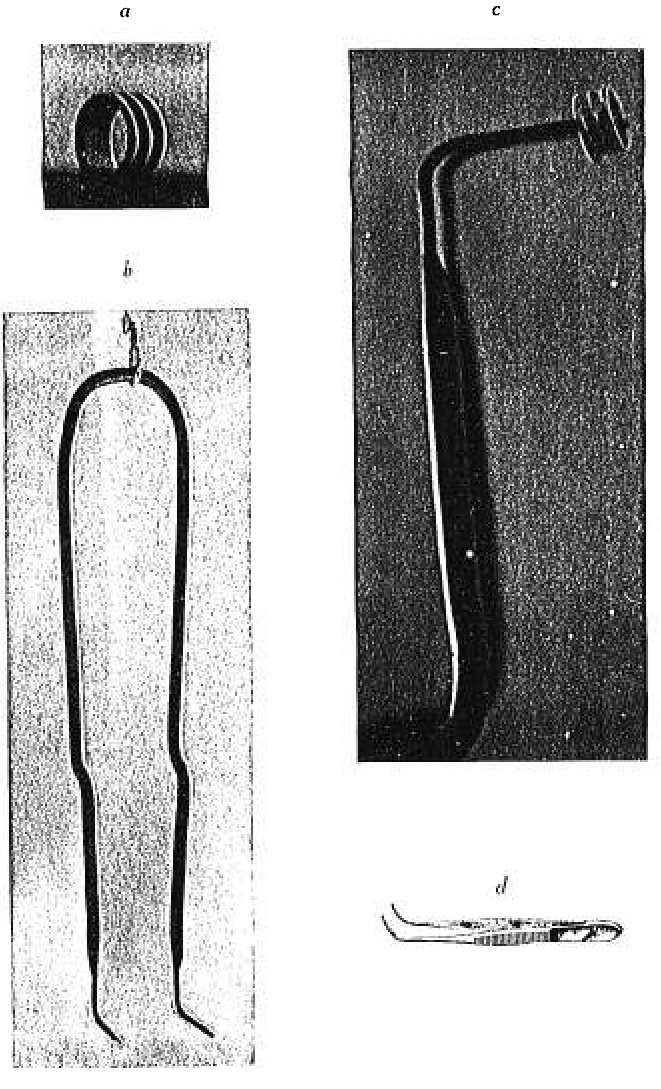
* Jaeger prize essay for 1907, at the German Hospital, New York.

[1] New York Medical Journal, Dec. 22, 1906.

PLATE I.



Instruments required for direct transfusion; *a*, the connecting ring; *b*, the tongs for manipulating the ring; *c*, the ring held by the tongs ready for insertion; *d*, fine forceps for use on the vessels.

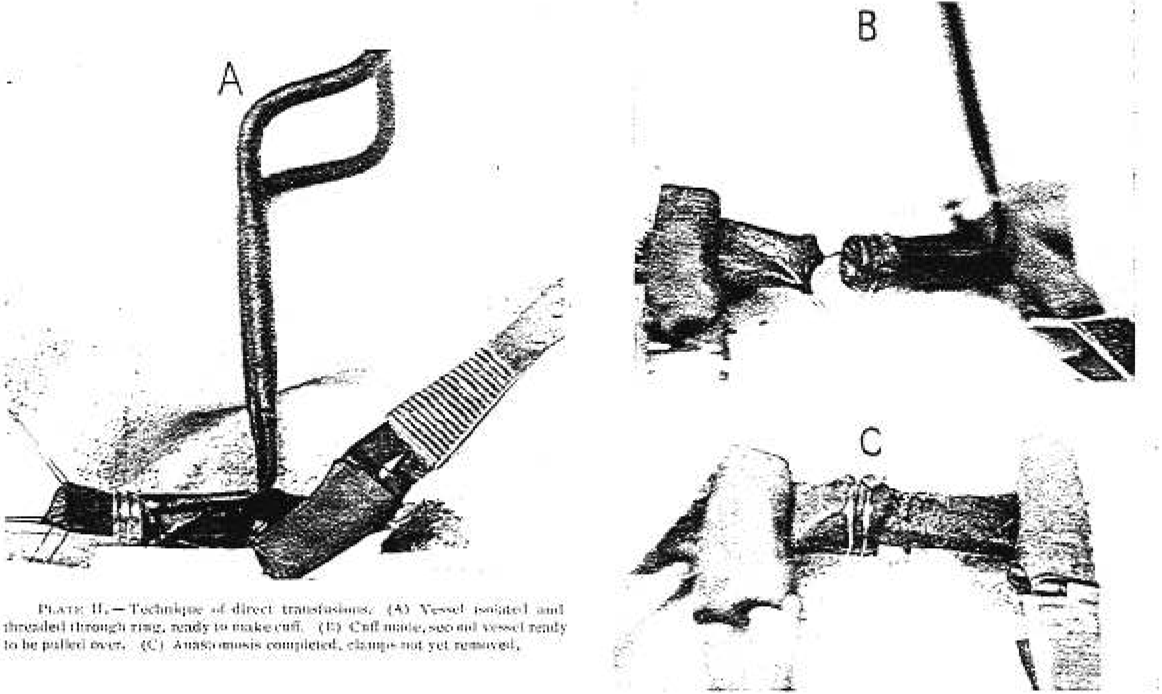


PLATE II.—Technique of direct transfusions. (A) Vessel isolated and threaded through ring, ready to make cuff. (B) Cuff made, second vessel ready to be pulled over. (C) Anastomosis completed, clamps not yet removed.

successful, the three failures could be traced to very definite causes; and the results should, therefore, be of value.

The method (Plates I and II) is extremely simple. It consists in the use of a small silver ring whose surface has two grooves.[2] The ring is held by a self-retaining spring forceps, which greatly facilitates the procedure.[3] The cut end of one of the divided vessels to be anastomosed is pushed through the ring and turned back over it like a cuff (see Plate II). This cuffing is very easily done if the open lip of the vessel is caught at three points in its periphery by three tension sutures of fine silk.

This cuff is then tied in place by a piece of fine silk in the posterior groove, and the other vessel is pulled over it. Then at once the two vessels are fastened together, intima to intima, by two fine pieces of silver wire, which fit into the two grooves. Silver wire is easy to put in place, and is absolutely certain not to slip, whereas silk, which was tried in the preliminary experiments, and which is recommended by previous writers, slipped in two of those experiments.

There are several points in technique, which, though small, are essential.

1. The vessels must be handled with the greatest possible gentleness, and must never be grasped with toothed forceps. Violation of this rule was the cause of failure in experiment No. 1 (*vide infra*). The best instrument for handling vessels is a fine bent forceps, known to eye surgeons as "curved foreign body-forceps," or "blood clot forceps" (see Plate 1, d).

2. The part to be cuffed back has to be prepared by carefully cleaning off adherent connective tissue. This is best done by pulling the connective tissue sheath over the cut end and snipping it off with scissors. On the end which is to surround the cuff, it is best to leave considerable connective tissue.

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[2] These rings were made for me by John Frick, No. 8 Liberty Place, New York.

[3] This clasp was made, after the author's design, out of one piece of one-eighth inch steel wire, by Mr. E. Foy, former assistant engineer of the German Hospital.

3. Throughout the procedure, the vessels must be kept moist with normal saline solution.

4. About one inch of the vessel to be cuffed, and about one-half inch of the vessel to be pulled over the cuff, is all that one need expose. The part to be cuffed back is easier to manipulate if free from branches. If branches cannot be avoided, they must be tied close to the vessel, with fine silk.

5. The ring must be of exactly the right size; that is, its lumen must be just as large as the outer diameter of the vessel to be cuffed back, when full of blood. If one vessel is larger than the other, the ring should be put on the smaller of the two.

6. As in all plastic operations, there must be no tension. (Tension was the cause of failure in one of the preliminary experiments.)

7. The part to be operated on, must, so far as possible be immobilized after operation. For this reason all experimenters on dogs report a far larger proportion of successes with the vessels of the neck and interior of the body, than with those of the extremities. (See experiment No. 4 below.)

8. The best means of temporary blood stasis is the use of Billroth's hare-lip clamps, well protected with soft rubber tubing (see figures).

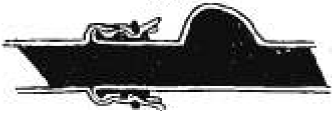
9. Sometimes the muscular sheath of the vessel contracts so as to render the procedure difficult. When this occurs, the muscle may be made to relax by application of hot saline solution, or the lumen may be gently dilated with a small hemostatic forceps.

10. Absolute asepsis is essential.

The first experiment.—Under ether, the right common carotid artery of a medium sized black dog was cut through and reunited. Only one silver wire ligature was placed around the ring.

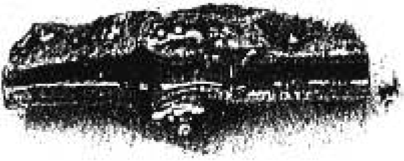
Five and a half days later, a small hemorrhage was seen from the wound, (which had united by primary intention). After about eight hours the dog was narcotized, the anastomosis was exposed and removed. The point of anastomosis, itself, seemed in good condition; the ring was in place, and the wire had not cut through. About one-quarter inch to the cardiac side of the ring was a small rounded swelling, which

FIG. 1.



Ring anastomosis of carotid artery; traumatic aneurism in cardiac side of ring.

FIG. 2.



Longitudinal section showing result obtained by ring anastomosis of carotid artery.

FIG. 3.

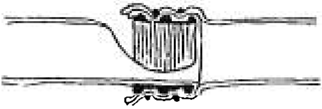


Diagram showing tear in wall of vessel from pressure of ring used in anastomosis of femoral artery.

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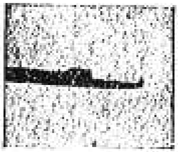

had ruptured at its apex, (see diagram), and was filled with fresh clotted blood (Fig. I). This was evidently the source of the hemorrhage, as no other source could be found. This traumatic aneurism was undoubtedly caused by the mouse-tooth forceps, which were used in this experiment, (but not in the later ones).

The second experiment.—The right common carotid of a fair sized hound was cut through and re-united; a silver wire was placed over each of the two grooves.

The wound healed and the dog remained in good condition. Three weeks later the dog was etherized and the anastomosis exposed. It was in perfect working order; the pulse in the vessel was almost, but not quite, as strong above the ring as below. The entire vessel was surrounded by a dense mesh of connective tissue which buried it securely. The segment of vessel was then removed, and experiment No. 3 was at once done on the same dog.

The segment removed, easily allowed water to be squirted through it; but, a day later, as the result of hardening in formalin, its lumen had so narrowed that a probe could not be passed through.

On closer inspection, after the specimen had been split longitudinally, (see Fig. 2), the lumen was seen to be clear but slightly contracted. There was an exceedingly fine line of organized blood clot between the two intimas, in the receding angle where they met. The wires had shown no tendency to cut through. The cuff and its envelope were losing their identity and becoming transformed into connective tissue.

The third experiment illustrates the result of even slight infection:—After the preceding specimen was taken out, the right internal jugular vein was exposed through the same wound, cut through, and quickly anastomosed. The largest ring at hand was about one-eighth inch too small for the vein, but was used. Toward the end of the operation several errors in asepsis were noted. One week later, the wound, which had united, was opened. The vessel was found, surrounded by a large pocket of serous exudate. The lumen of the vein at the point of anastomosis was closed by a ragged thrombus.

The fourth experiment.—The right superficial femoral artery of a fair sized dog was cut through and re-united. The entire operation, from the first incision to the last suture, took forty-five minutes.

Five days later, the dog was in good condition. The pulse in the right dorsalis pedis was exactly as strong as in the left. The dog was then allowed to run in the yard with the other dogs. The next day there was a hemorrhage from the wound. The dog had been very lively, and had attempted to jump over the fence at some rabbits in the next enclosure. On examination of the anastomosis, two thirds of the circumference of the vessel appeared to have torn on the edge of the ring, at the place where the cuff turned back (See diagram Fig. 3).

The chief dangers to be feared, then, are hemorrhage, thrombosis, and narrowing.

Hemorrhage ought never occur, provided that trauma to the vessel is avoided, and the part operated on is immobilized.

The prime causes of thrombosis are injury of the intima and infection; and elimination of these causes is merely a matter of technique. Narrowing of the lumen (which occurred in experiment No. 2, and in Jensen's experiments), can be avoided by the use of the proper sized ring. For this purpose, it is advisable to have a series of rings, in diameter from two millimeters up, and differing by about a half millimeter.

One other danger might be thought of—the occurrence of pathological changes after a considerable time, as the result of the presence of a rigid foreign body, or as the result of the abnormal anatomical relationships of the structures of the vessel wall, at the site of anastomosis. Whether such changes would occur can, of course, only be definitely settled by prolonged observations. But there seems no reason to believe that such a foreign body, imbedded in the scar tissues around the healed vessel, would do any harm. In those of Höpfner's experiments, in which the magnesium rings were not found absorbed, they had done no injury at the end of eight weeks. Silver wire sutures have, of course, been known to stay in the body for years. For these reasons it does not, at present, seem essential that absorbable materials be used.

The use of a ring external to the vessels, in blood vessel anastomosis, was first suggested by Nitze, at the International Medical Congress, at Moscow, in 1897.[4]

The first actual experiments on record were done by Payr,[5] in 1900, and the method is generally known by his name. He used rings of magnesium (which is very slowly absorbable in the body), and had very good results: though he did a large number of experiments, he did not give the details of them. Later, he reported one operation on the femoral vein of a man. The vessel was patent three days later when the patient died of pneumonia.

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[4] Centralblat f. Chirurgie, 1897, p. 1042.

[5] Archiv f. klin. Chirurgie, lxii, 1900, p. 67; lxiv, 1901, p. 726; lxxii, 1904, p. 32.

Jensen,[6] in 1903, experimented with several methods. His results were slightly in favor of suture methods and may be summarized as follows:—

With Arteries:	Bone Protheses.	Suture.
Perfect Result.		Two Cases.
Narrowing.	Three Cases.	Three Cases.
Thrombosis.		Seven Cases.

With Veins:	Various Protheses.	Suture.
Perfect Result.		One Case.
Narrowing.	Two Cases.	Two Cases.
Thrombosis.	Eight Cases.	Four Cases.

Jensen's results, so far as the ring method is concerned, are not conclusive, because he experimented with many different varieties of rings.

The most extensive work with magnesium protheses (or rings) is that of Höpfner, in von Bergmann's Clinic, in 1903.[7] He used the method altogether twenty-eight times, in different experiments on dogs. Six were simple end-to-end anastomoses. Of these, two thrombosed (both of them with two millimeter rings): while, of the four successful cases, two were with three, and two with five millimeter rings. He also did six reversal or transplantation experiments, with the carotid and femoral arteries. Of these, four were successful; two thrombosed on account of the small size of the vessels. His transplantation experiments with veins all failed. He concludes that the method is not applicable to vessels smaller than three millimeters in diameter.

That blood vessels can be permanently united, by the ring method, is undoubted. Whether this method presents any advantages, excepting its simplicity, over the suture methods, is doubtful, and remains to be determined by further work. The method has been little known and nobody but Höpfner and Payr has used it often enough to become expert at it. The suture method, on the other hand, has been perfected by a long series of experiments; and the author has had the pleasure of witnessing the finished skill with which Dr. Carrel performs his operations.[8]

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[6] Copenhagen. (Quoted from Watts.)

[7] Archiv f. klin. Chirurgie, lxx, 1903, p. 417.

One thing, however, is certain,—that for the temporary anastomosis necessary in direct transfusion, the ring method, because of its simplicity, is the method of choice.

Clinical Experiences in Transfusion.—In October, 1907, the author had the opportunity to perform transfusion in two desperate cases of secondary anæmia. While the immediate results were very satisfactory, both cases terminated fatally from continuation of the original diseases.

CASE I.—The first case was one of hemorrhages of obscure etiology. The patient, a German girl of twenty-five years, a trapeze performer, was admitted to the German Hospital, on the medical service of Dr. Morjé, Sept. 26, 1907.

Except that one of her sisters suffered from prolonged and profuse menstruation, there was no indication of any tendency to hemophilia in the family history. Her only previous illness was an attack of acute articular rheumatism, four years before her present trouble. Aside from rather frequent nosebleeds as a young girl, she had never suffered from bleeding of any kind. Her menstruation, which had begun at the age of twelve, was previously perfectly regular and normal, seldom lasted more than two days, and never was profuse. She had never been pregnant, and denied all venereal infection. Her illness dated back fourteen months, to an injury in a trapeze accident. She fell twenty-three meters into a net, and was unconscious; how long, she did not know. From that time on, she had had almost continual bleeding from the vagina. Four months before her admission to the hospital, a curettage had been performed. The bleeding had stopped for three weeks after this, and then had returned and continued. Aside from this, she had suffered, ever since the accident, from very frequent vomiting, which generally came on ten or fifteen minutes after meals. The vomitus was food just eaten and mucus, never blood. For two weeks before admission to the hospital, she had suffered with severe dyspnœa, cardiac pain and palpitation, and a bad cough (with small amounts of mucus sputum, never blood); and her legs had become swollen.

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[8] A careful study of the suture of blood vessels, with special reference to Carrel's work, will be found in an article by Watts, in the Johns Hopkins Medical Bulletin, May, 1907. Watts gives a full Bibliography. Carrel first described his method in the "Lyon Medical," 1902, vol. i, p. 859, and vol. ii, p. 114 and 153, and has published numerous articles since.

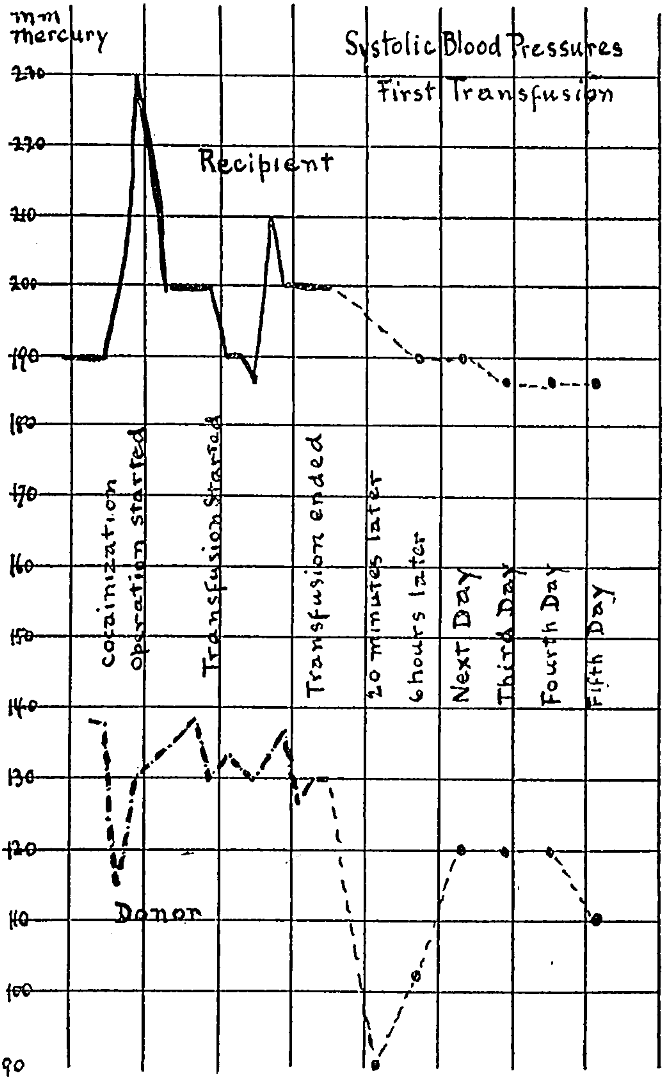
Examination, after admission, showed a very anæmic girl with œdema of the face and legs. There were signs of a bronchitis, and of well marked aortic and mitral insufficiency. The pulse approached the Corrigan type, and the blood pressure was abnormally high (200 mm.). She was bleeding from the vagina. The uterus was firm and freely movable, and there was a tough, cord-like blood clot hanging from the cervix. Ovaries and tubes were normal. Urine examinations were negative, and the blood examination showed a marked secondary anæmia (35 per cent. hemoglobin, 2,350,000 red blood cells).

In spite of every variety of local and general treatment, the bleeding continued, the vomiting became worse, so that the patient had to be supported by hypodermoclysis and rectal feedings, and the anæmia became more and more severe. On Oct. 11th, the patient seemed to be in extremis. She had taken practically no food for several days, and had signs of threatened œdema of the lungs. The hemoglobin had sunk to 15 per cent., and there were only half a million red blood cells to the cubic millimeter.

On Oct. 12, 1907, transfusion was performed. The donor of blood was a healthy girl of twenty-three years, who was paid by the patient's friends. The patient and the girl lay on tables, side by side, their heads in opposite directions. With the coöperation of Dr. F. Torek, the left radial artery of the donor, and the anterior ulnar vein of the patient were exposed, and their central ends united by exactly the same technique described above, for arterial anastomosis. Local anesthesia, by Schleich's infiltration method, was used. (The patient and the girl had had morphine before the operation.) Blood was flowing from the girl into the patient, exactly twenty-five minutes after the first incision.

As soon as the hare-lip clamps were taken off, the vein was seen to distend with blood, and could be felt to pulsate for several inches up the arm. The transfusion was allowed to continue for thirty-five minutes. Then, though both donor and donee were in excellent condition, it was thought best, following Crile's

PLATE III.



Showing blood pressure in recipient and donor in Case I of transfusion.

advice, to stop. Both vessels were then ligated, the anastomosed segments of vessel cut out, and the wounds closed by suture.

During the course of the transfusion, the condition of the patient improved visibly. Her lips, which had been pallid, became red; her breathing, which had been labored, became easier; her mental condition changed from semi-stupor to almost exhilaration; her blood pressure, which was observed every five minutes throughout the procedure, did not, on the whole, show any marked rise,—probably because it was already pathologically high. (See accompanying chart.)

The next day, the vomiting, which, up to this time had been uncontrollable, stopped. Blood examination, four hours after the transfusion, showed a rise of the hemoglobin from 15 to 35 per cent., and of the red blood cells from 600,000 to 1,096,000 per cubic millimeter.

This increase continued steadily, so that nine days later, the hemoglobin was 45 per cent. and the red blood cells 2,850,000 per cubic millimeter. The explanation of this continued rise in the blood count, after the transfusion, is probably that the total volume of blood was then abnormally high, and that in bringing the total volume back to normal, the body simply got rid of the excessive fluid part, so that the blood became more concentrated.

In spite of this improvement in the general condition, and in spite of every effort of the gynecologists, to whose charge the patient was now transferred, the bleeding from the uterus continued. Very tight packing of the uterus checked the hemorrhage for only a short time. Every other means for treating hemorrhage having been tried without effect, it seemed that in extirpation of the uterus lay the only hope for the patient's life; and accordingly, on Oct. 22nd, ten days after the transfusion, a hysterectomy was performed by Dr. F. Krug. The uterus and adnexa, removed, showed no gross lesions.

The loss of blood was slight, and the patient stood the operation well; but eight hours afterwards, bleeding from the vaginal wound began, and continued slowly, but steadily, until her death. The day after the operation, bleeding from the abdominal wound was noted; the superficial part of the wound was opened by Dr. Seeligman, the blood clots removed, and the wound sutured tightly again. Bleeding from this source then ceased.

Three days after the operation, vomiting commenced again

TRANSFUSION I. BLOOD EXAMINATIONS OF PATIENT.

To illustrate gradual rise in hemoglobin and red blood cells after transfusion.

	September 27.	October 8.	October 12.	October 12.	October 13.	October 15.	October 17.	October 19.	October 21.	October 30.
			Before transfusion.	4 hours after.						(Day before death.)
Hemoglobin	35%	20%	15%	35%	37%	45%	45%	40%	45%	25%
Red blood cells	2,350,000	560,000	600,000	1,096,000	2,064,000	1,744,000	2,220,000	1,840,000	2,850,000	1,500,000
Leucocytes	11,700	9,600	13,000	16,000	....	9,400	....	....	16,400	....
Polynuclear	82%	79½%	88%	91%	....	....	....	....	83%	....
Lymphocyte	14%	16%	10%	8%	....	....	....	....	13½%	....
Mononuclear	1½%	3½%	½%	½%	....	....	....	....	1%	....
Eosinophile	2½%	½%	½%	0%	....	....	....	....	2½%	....
Basophile	0%	0%	1%	½%	....	....	....	....	0%	....
		Microcytes. Poikilocytes. No nucleated red blood cells.								

and from this to the end, the same pernicious type of vomiting persisted; and, as the patient was unable to retain rectal feedings, she received practically no nourishment for the last seven days of her life. This, probably, more than the bleeding, which was not profuse, contributed to the fatal termination. For the last four days of her life, the patient bled from her gums, and the vomitus contained small amounts of blood (probably swallowed). All of the usual means of treating hemorrhagic conditions were of no avail.

At no time was there any evidence of lack of coagulability of the blood. There was no jaundice, no hemoglobinuria, or other symptoms to point to hemolysis.

The patient died on Oct. 31st, nine days after the hysterectomy, and nineteen days after the transfusion.

The effect on the girl, who gave her blood to this patient, should also be noticed. During the transfusion there was no visible change. Her pulse remained strong and slow, and the blood pressure dropped only 12 mm. (see chart). Twenty minutes after the end of the transfusion she suddenly became faint and pale, the blood pressure dropped 40 mm., and the pulse rate slowed to 60.

This condition was transient; but for six or eight hours the patient felt weak. She was able to sit up the next day, and on the fifth day was discharged from the hospital, none the worse for her experience. The change in her blood was small, the red blood cells dropping only from 3,400,000 to 3,000,000 per cubic millimeter, and the hemoglobin from 80 to 72 per cent. She went about and attended to her business, a week after the transfusion.

There was no data to determine the amount of blood lost. This could have been done, either by weighing the donor or patient, before and after the transfusion, or as Watts suggests, by cutting the vein at the termination of transfusion, measuring the amount of blood which flows from the artery through the anastomosis, in a given number of seconds or minutes, and from this, calculating the amount which has flowed in the time taken by the transfusion. (This method, it should be noted, has the error of not taking into account the resistance offered by the venous pressure of the donee.)

The second case in which a transfusion was performed, presented, like the first, so many clinical aspects of interest, that it is hard to refrain from discussing the case in detail.

CASE II.—The patient, a Hungarian, married, 52 years old, and a civil engineer, was admitted to the surgical service of Dr. Kiliani, Oct. 12, 1907. The family and previous history can be disregarded. The patient had never been ill in his life.

For a year and a half he had been suffering, at intervals, with severe epigastric pains, and had been growing progressively weaker. During this time he had lost about forty pounds. For two months he had been vomiting frequently, generally at once after eating. He had never noticed blood in the vomitus.

The principal points in the physical examination were: marked cachectic appearance and emaciation; Argyle-Robertson pupil; Romberg's symptom, and absence of knee jerks; signs of a chronic bronchitis and of arterio-sclerosis; scaphoid abdomen, with marked tenderness and an indistinct mass in the epigastrium.

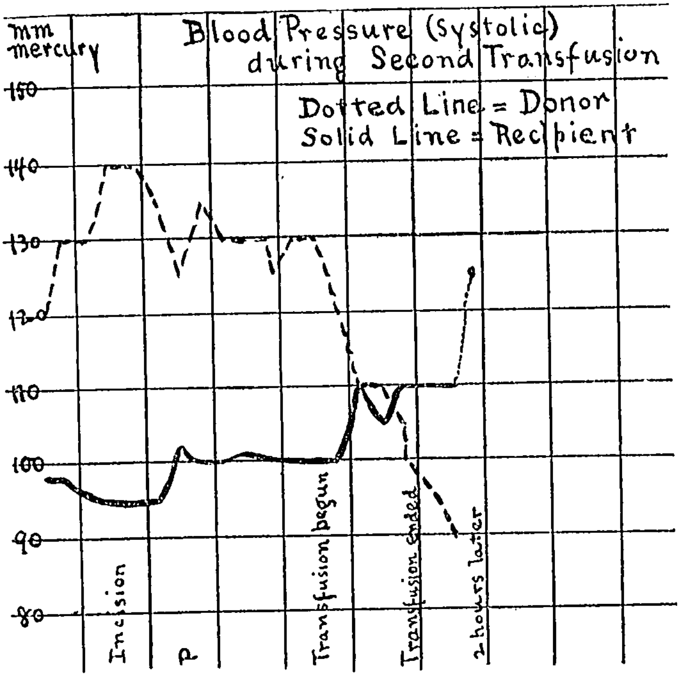
While in the hospital, the patient vomited, almost daily, large quantities (one to two pints) of altered blood. The vomitus, unexpectedly, turned out to contain considerable amounts of free hydrochloric acid. The stomach contents, too, after a test breakfast, showed free hydrochloric acid 45, total acidity 90. After the vomiting, the patient would feel much relieved for some hours; otherwise, he suffered from constant and severe pain, so that he had to be kept under the influence of opiates almost all the time.

As a result of the constant vomiting of blood, the patient's general condition steadily deteriorated; the red blood cells sank from 2,480,000 to 1,300,000, and the hemoglobin to 20 per cent. The diagnosis was in doubt. Although the acidity of the stomach contents was high, the cachectic appearance and the history of the case, pointed to carcinoma, rather than ulcer, of the pylorus. An exploratory laparotomy seemed indicated; but it was plain, that in the patient's weakened condition, any operation would mean death,—probably on the operating table.

Under these circumstances, a transfusion was thought of, for the purpose of restoring the patient to an operable condition. A ready donor was found in the patient's wife. She was a healthy woman, but undersized, weighing only 90 pounds. On this account, the transfusion from her was, at first, thought unwise. But, as she insisted on taking the risk, the operation was performed on Oct. 28th, at 10.30 A.M.

The anastomosis was made by Dr. Kiliani and the author, in the same manner as in the preceding case. Blood was only allowed to run over from wife to husband for 17 minutes. At the end of that time, the wife began to look pale and feel weak, and it seemed best to stop.

PLATE IV.



Showing blood pressure in recipient and donor in Case II of transfusion.

Even during this short transfusion, the general appearance and condition of the patient improved markedly,—in fact, much more, than the increase of red blood cells to 1,772,000 immediately after, as compared with 1,330,000 per cubic millimeter just before the transfusion, would have led one to expect. The pulse became stronger, and the blood pressure rose 10 mm. during the transfusion. (See chart.) At the beginning of the transfusion the patient lay weak and depressed, comforted by his wife. After it, the reverse was true, and the patient, whose spirits were almost buoyant, became the comforter. (There is, no doubt, an element of suggestion in this marked mental change, which is described in nearly all cases of transfusion.)

It was considered best to operate at once, before the patient could, by further hemorrhages, lose the blood thus given. At two o'clock of the same day, an exploratory laparotomy was performed. A tumor, involving the lesser curvature of the stomach, and adherent to liver and pancreas, was felt. As the condition appeared to be a hopelessly inoperable carcinoma, the abdomen was closed at once. After the operation, the patient gradually sank, and he died three days later of exhaustion.

Post mortem, was found, near the pylorus, a large, round ulcer, in whose base was seen the patent blood vessel, from which the fatal hemorrhages had taken place. The whole pyloric end of the stomach formed a greatly thickened and indurated mass of carcinoma, which was densely adherent to pancreas and liver.

The wife suffered very little inconvenience, and was discharged from the hospital on the second day. During the transfusion her blood pressure dropped 10 mm. The red blood cells dropped only from 4,400,000 to 4,000,000 after the transfusion, and the change in the hemoglobin was not enough to be measured.

The history of transfusion is a remarkable story of alternate enthusiasm and rejection. It will only be briefly reviewed here.[9]

Though there are many doubtful accounts, there is no clear evidence that any actual transfusion was tried before Harvey's discovery of the circulation of the blood, in 1628. Shortly after this, Christopher Wren [10] first conceived the idea of injections into blood vessels (infusion), and the first experimental transfusions were done on dogs by Richard Lower.[11]

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[9] The history up to 1875, is fully given in Landois' "Die Transfusion des Blutes," Leipzig, 1875. Köhler, in "Gedenkschrift f. d. verstorben. Generalstabsartzt v. Leuthold," Berlin, 1906, p. 269, brings the history to 1906, with certain omissions.

[10] Philosophical Transactions, vol. i, 1665, p. 128. (Landois.)

[11] Philosophical Transactions, vol. i, 1666, p. 352. (Landois.)

The first transfusion on a human being was done by Jean Denis, in France, 1666. In the years following, transfusion was tried everywhere, with much eagerness and controversy. Some of these transfusions were from animal to man, others from man to man; some of them were direct from vessel to vessel, by means of a cannula; but most of them were indirect; *i.e.,* some sort of pump or container was used. Some successes were reported; but there must have been many failures or fatalities, because the procedure was dropped within a few years, and hardly heard of again for over a century. It was even forbidden by the French government.[12]

In the beginning of the 19th Century, transfusion was again taken up. Blundell[13] reported seven cases of transfusion of human blood, of which three ended in recovery. Scheele[14] in 1802, and Diefenbach[15] in 1828, wrote extensive reviews of the subject. Dumas and Prevost[16] first showed the injurious effect of the blood of one species on that of another: and most of the transfusions of this period were from man to man. Bischoff,[17] about 1835, introduced defibrination; Diefenbach[18] in his second work on transfusion in 1848, advised defibrination. This method then became the established procedure, and Panum[19] and Brown-Sequard,[20] as the result of numerous experiments, both state that it is the main point in successful transfusion.

In the middle of the century, numerous scattered cases were reported; and in 1863, Blasius[21] collected all the transfusions of the previous forty years,—116 in all, 56 with report of good results. Of these, all were indirect transfusions; only two were from animals (both said to have been successful):

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[12] Dorsett, Interstate Med. J., 1906, p. 217.

[13] Lancet, vol. 9, Oct., 1825.

[14] Copenhagen, 1802.

[15] "Ueber die Transfusion des Blutes," Berlin, 1828.

[16] Ann. de Chimie, 1821, p. 294.

[17] Müller's Archiv, 1835.

[18] Rust, Handbuch der Chirurgie, vol. iv.

[19] Virchow Archiv, xxvii.

[20] Journal de la Physiol, 1858.

[21] Deutsche Klinik, 1863.

and the fourteen cases with undefibrinated human blood, were unsuccessful. Some of the fatal accidents were attributed to air embolism. (Lowenthal[22] showed, in 1871, that small amounts of air in the circulation do no harm and are absorbed.)

For the twenty years between Blasius' publication and an important publication of von Bergmann's in 1884, transfusion was a subject of great popular interest as well as of much scientific controversy. Great things were expected of it, and all sorts of exaggerated claims made. It was recklessly tried, not only in anæmia, but in every form of disease. Emerson[23] in one of his essays, refers to it as "the boldest promiser of all,—the transfusion of the blood,—which, in Paris, it is claimed, enables a man to change his blood as often as his linen!"

New and complicated methods were devised, and many cases were described. In the Franco-Prussian war, thirty-seven transfusions of defibrinated human blood were reported, of which thirteen were said to have been successful.[24] The books and articles on the subject appearing in this period are very numerous. Geselius[25] and Hasse[26] reintroduced transfusion from animals to human beings. Lambs blood was generally advised, because its red blood cells were smaller than those of man. The febrile reaction, hæmoglobinuria, and other symptoms, which regularly appeared in these cases, were regarded as merely incidental. All these attempts at transfusion of heterogeneous blood were given up, after Landois' discovery[27] that the red blood cells are absolutely destroyed and dissolved, when injected into a different species of animal. Ponfick,[28] some years later, 1883, in his studies of hæmoglobinæmia, gave the explanation of the previously noted symptoms which appeared in heterogeneous transfusions.

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[22] Berl. Klin. Wochenschr., 1871, No. 47.

[23] "Works and Days," 1870.

[24] Köhler, Loc. cit.

[25] "Zur Thierblut Transfusion beim Menschen," 1874.

[26] Arch. f. Path. Anat., vol. 64, 1875, p. 52.

[27] "Die Transfusion," Leipzig, 1875.

[28] Virchow Archiv., vol. 62.

Panum,[29] Landois[29] and many others proved, however, that blood may functionate normally, if transfused into an animal of the same species. In one of Panum's experiments, by repeated bleedings of one dog, with transfusions of defibrinated blood of other dogs, he exchanged practically all (over 99 per cent.) of the first dog's blood for that of the other dogs, and yet, the animal remained perfectly healthy.

That defibrination itself, carried dangers, now came to be recognized. Magendie[30] had already noted dyspnœa, diarrhœa and bloody exudates in the serous cavities after transfusion of defibrinated blood, and had warned against defibrination. A. Köhler,[31] in 1877, made the important discovery that intravenous injections of defibrinated blood or of serum, even in animals of identical species, might cause intravascular clotting (multiple thrombosis), because of the introduction of an excess of fibrin ferment. And Cohnheim[32] made the authoritative statement that injection of any blood, in which coagulation had already taken place, was an unpardonable error.

These things, together with the general introduction of intravenous infusion of saline solution, about 1875, caused transfusion to be gradually abandoned. And von Bergmann,[33] in 1883, gave transfusion what appeared to be its death sentence. He reviewed the whole subject, and came to the conclusion that the only reason there had not been more fatalities was, that in most cases not enough fibrin ferment had been introduced to produce extensive intravascular clots. He said that the only allowable transfusion was direct, from artery to vein; but that the method was uncertain and cumbersome, and coagulation was likely to occur in the cannula.

From that time, up to the present century, transfusion is scarcely heard of; and writers, who refer to it, even as late as

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[29] Loc. cit.

[30] "Lecons sur le Sang," Paris, 1838.

[31] "Ueber Thrombose und Transfusion," Dorpat, 1877.

[32] "Vorlesungen über algemeine Pathol, vol. i, 1877, p. 346.

[33] "Die Schicksale der Transfusion im letzten Dezennium," Berlin, 1883.

1904[34] and 1906,[35] all mention it merely as a matter of historic interest, leading up to the introduction of intravenous infusion.[36]

In the beginning of our century, transfusion may be said to have almost been rediscovered. Von Bergmann had laid down the conditions under which transfusion would be permissible; and, until recently, these conditions were not to be attained.

But, with the recent development of practical means of blood vessel anastomosis, direct arterio-venous transfusion again seemed to come within the realm of possibility. In 1898, Crile,[37] in Cleveland, began a series of experiments which he has continued up to the present, and with the most brilliant results.

At first he used suture methods to perform the anastomosis; but more recently, he has adopted the ring method, and has improved it by adding a handle to the ring. He has, experimentally and to some extent clinically, proved that transfusion is the best treatment for every degree of hemorrhage, as well as for surgical shock, and that (with certain possible exceptions to be mentioned later), the transfused blood suffers no impairment, and is a perfect substitute for the lost blood.

Crile has, up to date, reported seventeen clinical cases, of which the results are summarized as follows:

Positive: Acute hemorrhage, pathological hemorrhage (from prolonged jaundice), shock.

Negative: Pernicious anæmia, leukæmia, carcinoma, strychnine poisoning, diphtheria.

Doubtful: Chronic suppuration, tuberculosis, typhoid.

In all his cases, the immediate result was marked improvement in the patient's condition, with no injury to the donor. It also seems, from his experimental work, that transfusion will be curative in illuminating gas poisoning.

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[34] De Bruire, Wiener Klinik, xxx, 1904, p. 223.

[35] Köhler, "Gedenkschrift, etc." already cited.

[36] Küttner, Beiträge z. klin. Chirurgie, 1903, p. 609.

[37] Journ. Am. Med. Assoc., 1906, xlvii, p. 1482.
Proceed. Soc. Exper. Biol. and Med. iv, p. 6 and p. 64.
N. Y. Med. Journ., 1907, lxxxvi, p. 145.
Cleveland Med. Journ., 1907, vi, p. 112.
Canada Lancet, 1907, xl, p. 1057.
ANNALS OF SURGERY, 1907, xlvi, p. 329.

Recently Watts [38] has described four cases of transfusion, by the use of Carrel's suture. In one of these, probably very little blood was transfused, as an occlusive thrombus was found. In the other three cases, the amount of improvement was disappointing; but the cases were very unfavorable.

One point, whose importance has only lately become evident, remains to be discussed.

That the blood of one healthy animal is physiologically interchangeable with that of another healthy animal of the same species, is amply demonstrated. Whether the same is true, if one of the animals be diseased, is still an unsettled question. A recent report of a case of fatal hemolysis after transfusion,[39] Crile's and Watt's reports of destruction of red blood cells after transfusion in cases of pernicious anæmia, and the experimental results of Ascoli,[40] indicate that in some diseased conditions, mixture of blood produces hemolysis.

It is possible, by methods now known, to determine beforehand whether hemolysis is likely to occur when any two given bloods are mixed. Such an examination was made before the second transfusion described in this paper. A thing much to be desired is, that a convenient clinical test for this purpose be devised. A test of this kind, and a better knowledge of the diseases which contraindicate transfusion, should make transfusion one of the safest and most valuable of therapeutic measures.

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[38] Johns Hopkins Bulletin, May, 1907.

[39] Pepper and Nisbet, Journ. Am. Med. Assoc., Aug. 3, 1907.

[40] "Isoagglutinnine and Isolysinne menschlichen Blutes." Deutsche Med. Wochenschrift, 1901, p. 1239.